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Development and Evaluation of Controlled-Release Matrix Tablets of Quetiapine Fumarate Using Hydrophilic Polymers

Nalikiri Himasree[1], U. Supriya[2]*, G. Srinivasa Rao[3]

[1]*Student, Department of Pharmaceutics, Saastra College of Pharmaceutical Education and Research, Nellore, Andhra Pradesh, India.*
[2]*Associate Professor, Department of Pharmaceutics, Saastra College of Pharmaceutical Education and Research, Nellore, Andhra Pradesh, India.*
[3]*Professor and Principal, Saastra College of Pharmaceutical Education and Research, Nellore, Andhra Pradesh, India.*
***Corresponding E-Mail:** supriyapharmacy24@gmail.com*

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ABSTRACT
The present study aimed to develop controlled-release matrix tablets of quetiapine fumarate using various hydrophilic polymers to prolong drug release and reduce dosing frequency. Matrix tablets containing quetiapine fumarate were prepared by direct compression using hydroxypropyl methylcellulose (HPMC K15M and HPMC K100M) and guar gum as release-retarding polymers. Precompression parameters including angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio were evaluated. The compressed tablets were assessed for hardness, friability, thickness, weight variation, drug content, and in vitro drug release. The powder blends exhibited satisfactory flow properties. All formulations complied with pharmacopeial requirements for post-compression parameters. Drug release studies were performed in 0.1N hydrochloric acid for 2 hours followed by phosphate buffer pH 6.8 for 6 hours. Among the formulations, F2 containing HPMC K15M exhibited sustained drug release of 97.3% over 8 hours and demonstrated desirable controlled-release characteristics. Formulations prepared with higher concentrations of HPMC K100M showed slower drug release, whereas guar gum formulations failed to provide the desired release profile. The study concludes that HPMC K15M is an effective polymer for developing controlled-release quetiapine fumarate tablets.
Keywords: Quetiapine fumarate, controlled-release tablets, HPMC K15M, HPMC K100M, matrix tablets

INTRODUCTION

Oral drug delivery remains the most widely accepted route of administration because of patient convenience, cost-effectiveness, and ease of manufacturing. However, conventional dosage forms often require multiple daily doses, resulting in fluctuations in plasma drug concentration and reduced patient compliance. Controlled-release dosage forms are designed to release the drug at a predetermined rate, maintaining therapeutic drug levels for extended periods. Such systems reduce dosing frequency, improve patient compliance, minimize adverse effects, and provide more consistent therapeutic outcomes.

Quetiapine fumarate is an atypical antipsychotic agent used in the treatment of schizophrenia, bipolar disorder, and major depressive disorder. The drug possesses a relatively short elimination half-life of approximately six hours, necessitating multiple daily dosing. Therefore, quetiapine fumarate represents a suitable candidate for controlled-release drug delivery systems. Hydrophilic matrix systems employing polymers such as hydroxypropyl methylcellulose (HPMC) have been widely utilized for sustained drug release due to their safety, ease of formulation, and predictable release characteristics. The present investigation aimed to formulate and evaluate controlled-release matrix tablets of quetiapine fumarate using different grades of HPMC and guar gum.

METHODOLOGY

Materials

Quetiapine fumarate was obtained from Hetero Laboratories, India. HPMC K15M, HPMC K100M, guar gum, magnesium stearate, talc, and microcrystalline cellulose PH102 were used as pharmaceutical excipients.

Preparation of Matrix Tablets

Controlled-release tablets containing 100 mg of quetiapine fumarate were prepared by direct compression. The drug and excipients were blended uniformly and compressed using a rotary tablet compression machine equipped with 12-mm punches.

Table.1: List of Ingredients

INGREDIENT	F1	F2	F3	F4	F5	F6
Quitiapine fumerate	100	100	100	100	100	100
HPMC K15M	50	150	-	-	-	-
HPMC K100M	-	-	50	100	-	-
GUAR GUM	-	-	-	-	50	200
Talc	5	5	5	5	5	5
Mg. Stearate	5	5	5	5	5	5
MCC pH102	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
TOTAL	500	500	500	500	500	500

The powder blends were evaluated for:

- Angle of repose
- Bulk density

- Tapped density
- Carr's index
- Hausner ratio

Evaluation of Tablets

- The prepared tablets were evaluated for:
- Weight variation
- Thickness
- Hardness
- Friability
- Drug content
- In vitro dissolution studies

In-Vitro Dissolution Study

Drug release studies were conducted using USP paddle apparatus. The dissolution medium consisted of 0.1N HCl for the initial 2 hours followed by phosphate buffer pH 6.8 for the remaining study period. Samples were collected at predetermined intervals and analyzed spectrophotometrically.

RESULTS AND DISCUSSION

The calibration curves of quetiapine fumarate in 0.1N HCl and phosphate buffer pH 6.8 demonstrated excellent linearity with correlation coefficients greater than 0.998. Standard Calibration curve of Quitiapine fumarate: Concentration and absorbance obtained for calibration curve of Quitiapine fumarate in 0.1 N hydrochloric acid buffer (pH 1.2)

Table.2: Calibration results

S. No.	Concentration (µg/ml)	Absorbance* (at 298 nm)
1	2	0.193
2	4	0.34
3	6	0.461
4	8	0.579
5	10	0.709
Correlation Coefficient = 0.9985,y = 0.0636x + 0.0751		

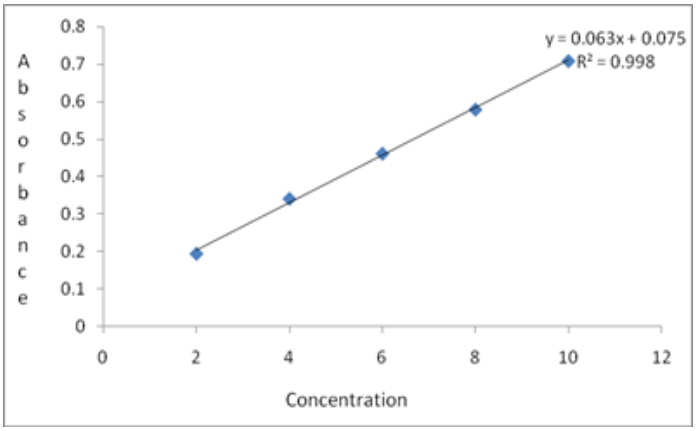

Fig.1: Calibration curves of quetiapine fumarate

Precompression studies indicated satisfactory flow characteristics of the powder blends. The angle of repose ranged from 26.7° to 29.3°, while Carr's index and Hausner ratio values suggested good compressibility.

The dissolution studies revealed that polymer type and concentration significantly influenced drug release. Tablets containing HPMC K15M exhibited effective release retardation and maintained drug release up to 8 hours. Formulation F2 demonstrated approximately 97.3% drug release after 8 hours and showed the most desirable controlled-release behavior.

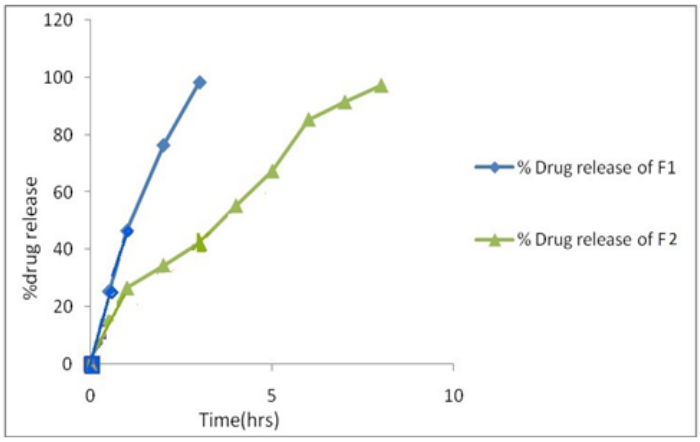

Fig.2: Dissolution profile of formulations prepared with HPMC K15M polymer

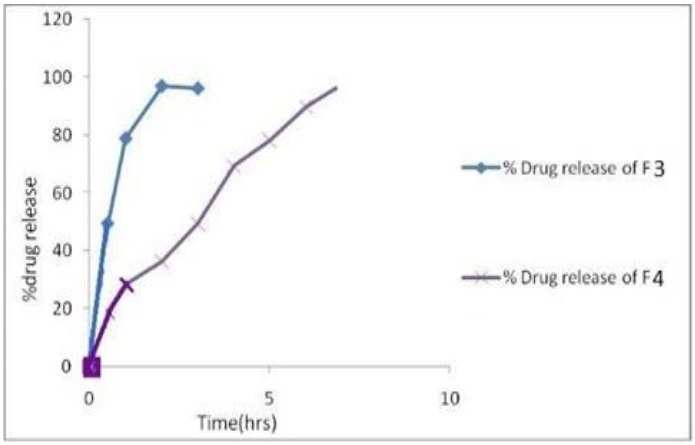

Fig.3: Dissolution profile of formulations prepared with HPMC K100M polymer

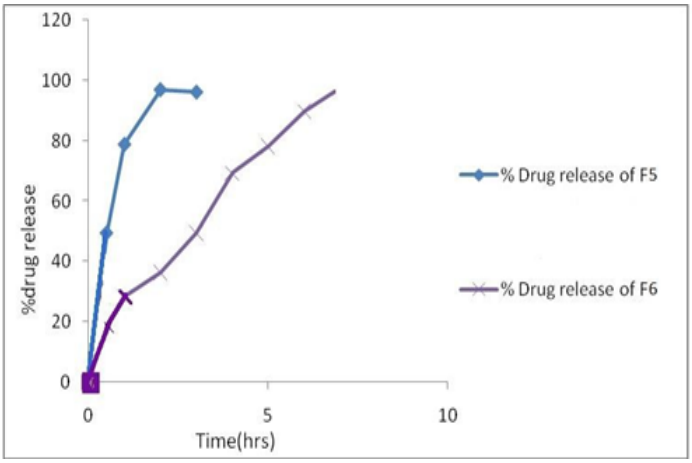

Fig.4: Dissolution profile of formulations prepared with Guar gum as polymer

DISCUSSION:

From the tabular column it was evident that the formulations prepared with HPMC K15M as retarding polymer in low concentrations the polymer was unable to produce the required retarding action to the tablets. As the concentration of polymer

increases the retarding nature was also increased. HPMC K15 M in the concentration of 150 mg showed good % drug release i.e., 97.3 in 8 hours. Where as in case of formulations prepared with HPMC K100 M as retarding polymer, the formulations with 50 mg concentration of polymer showed complete drug release in 6 hours only, whereas the concentration of polymer increases the retarding nature also increased. The Formulation Containing HPMC K100M in 100 Mg Concentration Showed good retarding nature with required drug release in 8 hours i.e., 82.3%.Where as in case formulations prepared with Guar gum as retarding polymer, as the concentration of polymer increases the retarding nature was also increased. When compared with HPMC polymers it was failed to produce desired drug release pattern. From the above results it was evident that the formulation F2 is best formulation with desired drug release pattern extended up to 8 hours.

Table.3: Pre-compression parameters

Formulations	Bulk Density (gm/cm^2)	Tap Density (gm/cm^2)	Carr's Index (%)	Hausner ratio	Angle of Repose(Θ)
F1	0.45	0.55	18.18	1.22	27.91
F2	0.50	0.58	13.79	1.16	29.34
F3	0.50	0.58	13.79	1.16	29.34
F4	0.47	0.55	14.54	1.17	28.23
F5	0.41	0.50	18	1.21	26.78
F6	0.41	0.54	18.11	1.22	26.71

Table.4: Post-Compression parameters

FD	Weight Variation(mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Assay (%)
F_1	494	4.5	5.5	0.43	97.23
F_2	510	4.2	5.5	0.49	98.16
F_3	502	4.3	5.5	0.49	98.16
F_4	508	4.3	5.5	0.34	98.55
F_5	506	4.4	5.5	0.34	99.25
F6	504	4.5	5.5	0.43	98.5

CONCLUSION

The present study successfully developed and evaluated controlled-release matrix tablets of quetiapine fumarate using hydrophilic polymers by the direct compression method. All formulations exhibited satisfactory pre-compression and post-compression characteristics, indicating good flow properties, acceptable mechanical strength, uniform drug content, and compliance with pharmacopeial quality standards. The in vitro dissolution studies demonstrated that both the type and concentration of polymer significantly influenced the drug release profile. Among all formulations, F2 containing 150 mg of HPMC K15M exhibited the most desirable controlled-release behavior, providing 97.3% cumulative drug release over 8 hours, thereby achieving sustained drug delivery with an optimal release pattern. In contrast, formulations containing HPMC K100M produced a slower release, while guar gum formulations were less effective in achieving the desired controlled-release profile. Overall, the findings suggest that HPMC K15M is a suitable hydrophilic matrix-forming polymer for the development of controlled-release quetiapine fumarate tablets, with the potential to reduce dosing frequency, improve patient compliance, and maintain therapeutic drug concentrations. Further stability studies and in vivo pharmacokinetic evaluation are recommended to establish the clinical performance and long-term stability of the optimized formulation.

CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

FUNDING

This study received no specific funding from public, commercial, or not for profit funding agencies.

AI TOOL DECLARATION

The authors declare that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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